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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,912	10/04/2004	Takahiro Ito	0020-5301PUS1	4489

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1609	

NOTIFICATION DATE	DELIVERY MODE
08/23/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/509,912	ITO ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 9-19* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The instant application is a 371 national stage entry of PCT/JP03/04745 filed April 15, 2003. This application claims benefit of foreign priority document JP 2002-112864, filed April 16, 2002. Claims 1-19 are pending in the application and examined on the merits herein.

Information Disclosure Statement

The information disclosure statement filed October 4, 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

Claim 8 is objected to because of the informality "or" is misspelled as "ore". Claim 17 is objected to because of the informality "citric" is misspelled as "ciric". Appropriate correction is required.

Claim 7 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Claim 7 is a multiple dependent claim that depends from

multiple dependent claims 4, 5, and 6. Accordingly, the claim has not been further treated on the merits.

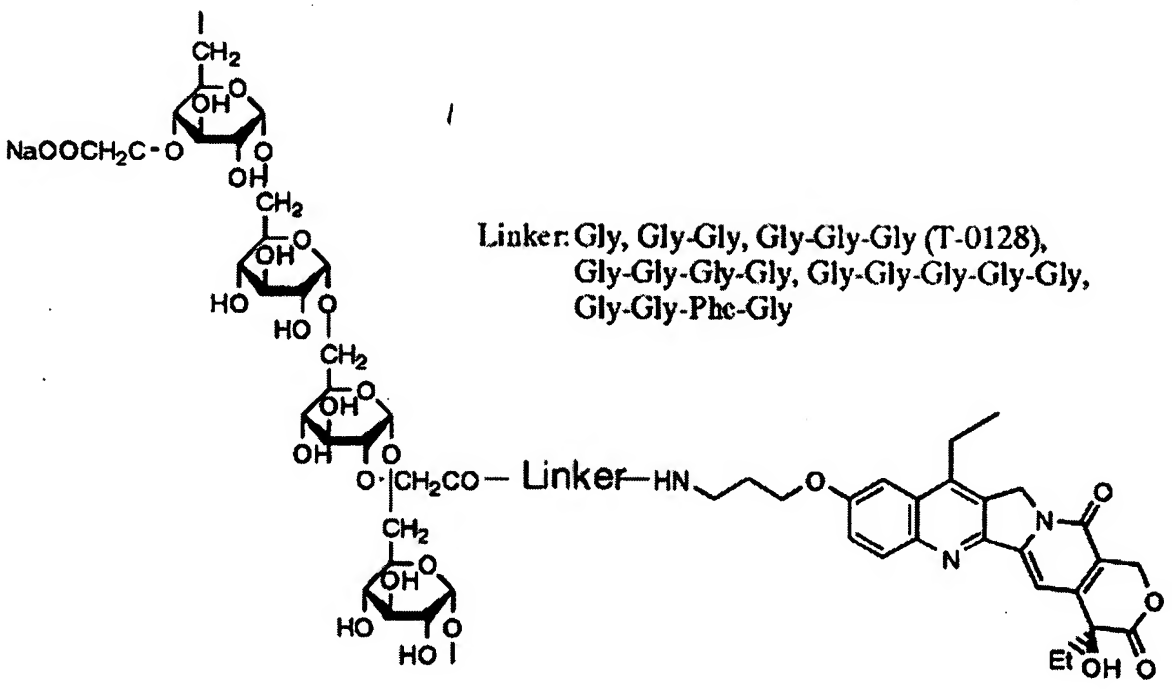
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8, 10-13, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Harada et al. (Journal of Controlled Release, 69, 2000, 399-412, cited in PTO-892).

Harada et al. disclose a "a novel [camptothecin] analog (T-2513: 7-ethyl-10-aminopropyloxy-[camptothecin]) bound to carboxymethyl (CM) dextran through a Gly-Gly-Gly linker." See abstract. Harada et al. discloses a liquid preparation comprising the camptothecin analog of the following formula



(Harada et al., page 401, figure 1) and an acetate buffer, reduced glutathione, EDTA, and Triton X-100, which can be interpreted to be stabilizers or fillers, at pH 4, as well as liquid preparations comprising the camptothecin analog adjusted to a pH range from 3 to 7 using acetate or phosphate buffers, optionally with $CaCl_2$, an alkaline earth metal chloride, added. The acetate or phosphate buffers are used at a concentration of 40 mM, which gives an ionic strength of less than 0.2. Harada et al. specifically disclose the camptothecin analog T-0128, wherein the linker is Gly-Gly-Gly. See Harada et al., page 401, figure 1, and page 402, right column, section 2.4. *In vitro evaluation of drug release*.

Claim Rejections - 35 USC § 103

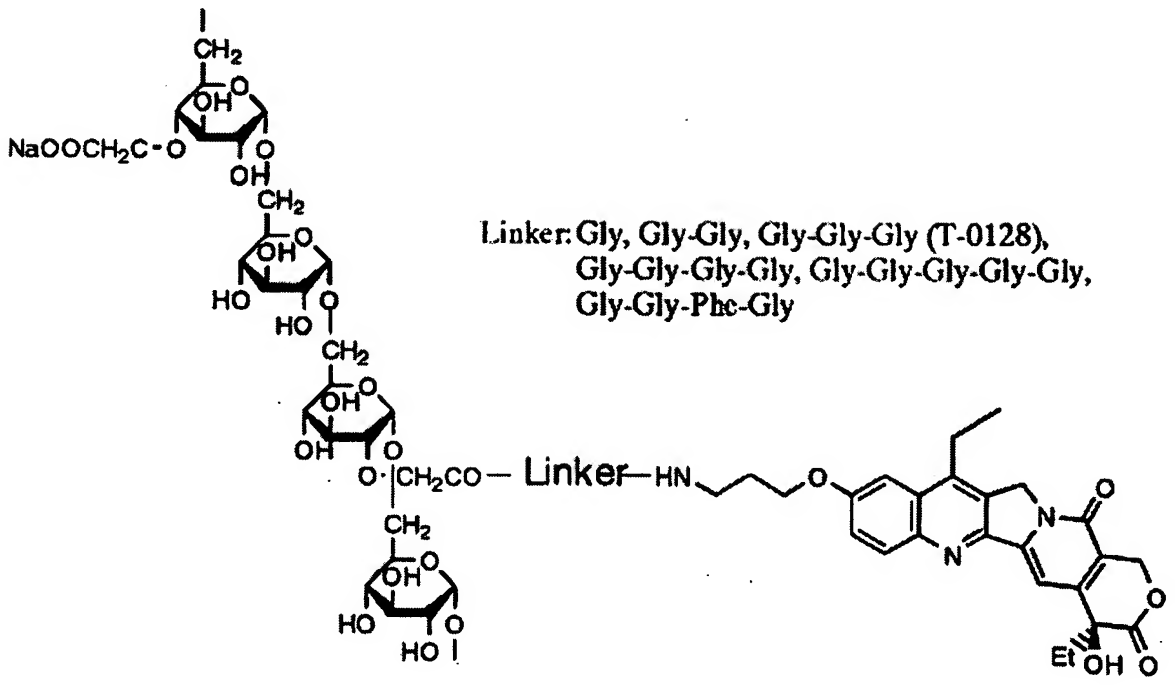
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9, and 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harada et al (Journal of Controlled Release, 69, 2000, 399-412, cited in PTO-892) in view of Wall et al (US patent 5,340,817, cited in PTO-892).

Harada et al. disclose a "a novel [camptothecin] analog (T-2513: 7-ethyl-10-aminopropyloxy-[camptothecin]) bound to carboxymethyl (CM) dextran through a Gly-Gly-Gly linker." See abstract. Harada et al. discloses a liquid preparation comprising the camptothecin analog of the following formula



and an acetate buffer, reduced glutathione, EDTA, and Triton X-100, which can be interpreted to be stabilizers or fillers. See Harada et al., page 401, figure 1, and page 402, right column, section 2.4. *In vitro evaluation of drug release*. However, Harada et al. does not disclose the use of alkali metal carbonates or alkali metal hydrogen carbonates as stabilizers or fillers such as lactose, sucrose, mannitol, dextran, maltose and trehalose. Harada et al. does not disclose the lyophilized drug composition prepared by lyophilizing the liquid preparation, not the liquid composition wherein the lyophilized drug composition is dissolved in an aqueous medium. Harada et al. does not disclose a liquid preparation wherein the buffer is citric acid and sodium hydrogen phosphate, optionally further containing sodium chloride.

Wall et al. discloses a camptothecin analog that is a water-soluble derivative of camptothecin bound to an amino acid or peptide. See column 8, lines 19-22. Wall et al.

discloses "the active ingredient may be incorporated into a solution or suspension. The solutions or suspensions may also include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic." See column 13, lines 14-27. Wall et al. also discloses oral liquid compositions, such as capsules, elixirs, suspensions, syrups, which generally include an inert diluent or an edible carrier and incorporated with excipients. See column 13, lines 29-36. Wall et al. discloses "following ingredients: ... an excipient such as starch or lactose, ... a sweetening agent such as sucrose". See column 13, lines 40 and 44. Wall et al. discloses the lyophilization of liquid preparations to provide the camptothecin derivatives. See column 18, lines 30-31 and 52-53. Wall et al. does not disclose the camptothecin analog disclosed in the instant application.

It would have been obvious to one of ordinary skill in the art at the time of the invention to adapt the use of pharmaceutical excipients in the pharmaceutical compositions of an amino acid- or peptide-bound camptothecin analog taught by Wall et al. to the liquid preparation of the camptothecin analog disclosed by Harada et al. For example, Wall et al. specifically discloses lactose and sucrose as pharmaceutical excipients.

It would have been obvious to one of ordinary skill in the art at the time of the invention to adapt the use of different buffers in the pharmaceutical compositions of an amino acid- or peptide-bound camptothecin analog taught by Wall et al. to the liquid preparation of the camptothecin analog using acetate and phosphate buffers disclosed by Harada et al. For example, Wall et al. specifically discloses citrates and phosphates as buffers, as well as sodium chloride as a tonicity adjusting agent.

It would have been obvious to one of ordinary skill in the art at the time of the invention to adapt the use of lyophilization of a liquid composition of a water-soluble amino acid-bound camptothecin analog taught by Wall et al. to the liquid preparation of the camptothecin disclosed by Harada et al. Wall et al. discloses in column 2 lines 2-5 need for additional water-soluble camptothecin analogs. One of ordinary skill in the art at the time of the invention would have a reasonable expectation of success in adapting this preparatory method due to the similarity between the amino acid-bound camptothecin analog taught by Wall et al. and the camptothecin disclosed by Harada et al.

Wall et al. further disclose "the active ingredient [prepared by lyophilization] may be incorporated into a solution or suspension. The solutions or suspensions may also include the following components: a sterile diluent such as water for injection..." See Wall et al. column 13, lines 14-17. It would have been obvious to one of ordinary skill in the art at the time of the invention to adapt the teaching of incorporating the camptothecin analog prepared by lyophilization into a solution of sterile water for injection taught by Wall et al. to the camptothecin analog disclosed by Harada et al.

Conclusion

No claims are found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Ardin Marschel can be reached on 571-272-0718 or Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSL

Cecilia Tsang

CECILIA TSANG
SUPERVISORY PATENT EXAMINER